

**MEPDEV 2<sup>nd</sup>: 2016**  
**Central & Eastern European LUMEN International**  
**Conference - Multidimensional Education & Professional**  
**Development. Ethical Values**

**The Usage Of Benzodiazepines By Medically Educated Persons In**  
**Macedonia**

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***Abstract***

The purpose of this paper is to show the frequency of usage of benzodiazepines in the Republic of Macedonia on the part of the population of medically-educated persons, as well as their attitudes, related to the use of benzodiazepines. This study is a segment of the huge cross-sectional study on 1328 respondents. It was conducted by students of the Higher Medical School in Bitola and students of the Faculty of Pharmacy in Skopje in different municipalities in the R. Macedonia (2013), limited to 410 respondents. The results were verified by appropriate statistical methods and tests. Of a total number of 410 respondents, benzodiazepines were consumed by 104 (18.47%), of whom 28 respondents (7.1%) without prescription. Stress (26.0%), insomnia (24.0%), anxiety (13.4%), etc., are considered the most common reasons for use of benzodiazepines. Medically educated people have an attitude that benzodiazepines cause harmful effects if used while driving and/or machine operating, and can cause both psychological and physical addiction ( $p < 0.05$ ). In recent years, the use of benzodiazepines in the R. Macedonia has been on the rise, they have been used by medically educated persons of various and younger age groups. If medically educated people use benzodiazepines despite their education about the beneficial and harmful effects of the use and abuse, it is necessary to analyze, which are the causes for maintaining this phenomenon, and which preventive measures should be undertaken in reducing the consequences.

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**Keywords:** Drugs, attitudes, benzodiazepines, medical education.



## 1. Introduction

Benzodiazepines have been frequently used and abused drugs for decades, particularly in countries where there is a possibility to easily obtain them without a prescription, only by displaying an identification card of a medical or health association. They are considered to be relatively safe drugs, often well tolerated by users (Mirchevska et al., 2014). Benzodiazepines are commonly used for relaxation of the muscles, facilitate insomnia problems, relieve anxiety, they are used in the treatment of panic attacks and obsessive-compulsive disorder with the expectation of improving the quality of life, reduction of the persistent chronic stress and solving family problems. The hopes of individuals, who use them without a physician's recommendation, are mainly to solve their psychical and psychological problems. Another group of users consume benzodiazepines for strengthening of the effects of another medicine, whereby prominent adverse reactions of benzodiazepines come to light. Especially after prolonged use of benzodiazepines their adverse reactions are more apparent and associated with concentration disturbance, lethargy and attention problems, for which their use is inadvisable during motor vehicle driving and/or operating machines. Further adverse reactions are problems with the memory, difficulties in movement coordination, and rare side effects such as seizures and hallucinations (Miletić, 2016; Nyström, 2005). Chronic abuse can cause psychological and physical dependence. The symptoms of these dependences may be increased in people who previously used narcotics and / or alcohol. In a sudden interruption of the consumption of these drugs the withdrawal symptoms may occur manifested as: emergence of anxiety, increased irritability and tension, muscle aches, tremors, insomnia, etc. Acute use of benzodiazepines in higher doses may result in dizziness, muscle relaxation, drowsiness, lethargy, coma and even death (Petrović, 2003; Lader, Tylee, & Donoghue, 2009; Uzun et al., 2005, p. 76; Uzun et al., 2010). In the Republic of Macedonia commonly used benzodiazepines (by their generic names) are: alprazolam, bromazepam, diazepam, klonazepam, lorazepam, nitrazepam, prazepam, etc.

## 2. Problem Statement

The diazepam drug, that belongs to the group of benzodiazepines in 2010 (Annual report for 2010, Ten most popular drugs in primary health care, 2010) in the list of most popular medication, located on the fourth and alprazolam on the eighth prescribed drugs.

From the data of drug utilization for 2011, according to Health Insurance Fund of Republic of Macedonia, (Annual report for 2011, Ten most popular drugs in primary health care, 2011) obtained in the Primary Health Care (PHC), the consumption of diazepam shifted from the fourth to third position, whereas alprazolam was on the ninth position.

In 2012, consumption of benzodiazepines, compared to 2011, are increased, but also was reported and for diazepam (Annual Report for 2012, ten most popular drugs in primary health care, 2012), Table 1.7, p. 5, 13), increases (2012/2011), to about 13.97%.

According to (Annual Report for 2012, ten most popular drugs in primary health care, 2012), fig. 11, p. 21, the drug diazepam, remains in third place, while alprazolam, moves to tenth place.

Among the ten most utilized drugs in 2013 ( Annual Report for the consumption of prescription drugs, from the list of drugs in Primary Health Care (PHC) for 2013, 2013), Fig. 14, p. 22) was diazepam,

a drug from benzodiazepine group, which was on the fourth place. Another benzodiazepine, alprazolam, the first time was not in the top ten most utilized drugs.

The average consumption of drugs in 2014 (Annual Report for 2014, ten most popular drugs in primary health care, 2014), fig. 18, p. 34, increased by 9%, compared to 2013. In the second place, according to number of prescriptions in 2014, were drugs acting on the CNS, with an increase of 10%, compared to 2013.

### **3. Research Questions**

For the purpose of this study a questionnaire containing 22 questions: structure of respondents according to gender and the use of benzodiazepines, relations of the most common reasons/indications for using benzodiazepines, the number of respondents-users respectively the reason and the number of nonusers, distribution of respondents according to responses of the way of obtaining benzodiazepines, structure of respondents regarding the use of benzodiazepines and driving/operating motor vehicle /machine, determination of the statistical significance among gender and attitude for the consumption of benzodiazepines during driving, distribution of responses by gender about the participants' view of whether benzodiazepines can cause psychic and physical dependence, determination of statistical significance among the gender and attitude of respondents whether benzodiazepines may cause psychological and physical dependence, statistical significance among the gender and attitudes of respondents about certain questions in the questionnaire (cross-data), was composed, and the data were collected electronically and in printed version.

### **4. Purpose of the Study**

The purpose of this study was to investigate the use of benzodiazepines among medically educated persons in the Republic of Macedonia and involving their attitudes. For that purpose a questionnaire was created and according to certain modalities in it, the data were utilized for: determination and presenting the use of benzodiazepines according to the gender (men/women) at the age of 18 to 65, and the level of medical education; determination of the status and variations of the use of benzodiazepines in the Republic of Macedonia; determination of the public awareness about this issue; applying the data obtained from the questionnaire to determine the existence of statistical significance between the gender and the use; during pregnancy and breastfeeding; before and during driving and / or machine operating and etc., to make a comparison with other similar studies.

### **5. Research Methods**

The subject of this analysis are medically educated persons (students in their ongoing education and graduated health professionals), applying an epidemiological method (cross-sectional study), and a health-statistical method, using appropriate statistical tests.

### 5.1. Place and time frame of the study

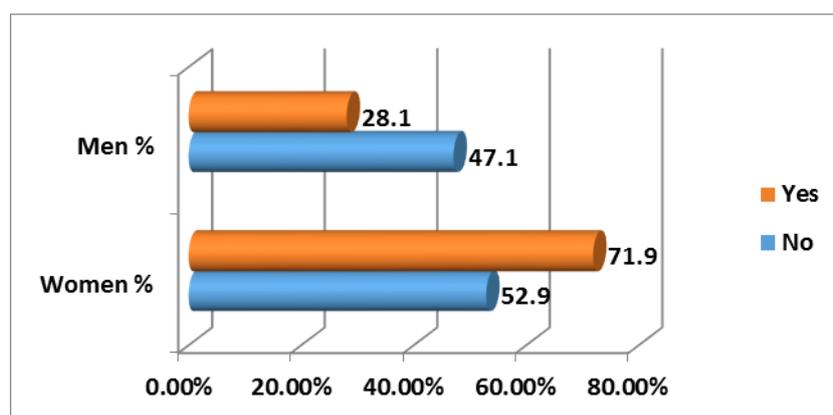
The study was conducted by students of the Higher Medical School in Bitola and the Pharmaceutical Faculty in Skopje, polling the student population in the Higher Medical School in Bitola, students of the Faculty of Pharmacy in Skopje and medically educated citizens on the territory of the Republic Macedonia in the municipalities of: Bitola, Demir Hisar, Prilep, Kichevo, Resen, Ohrid, Skopje, Kumanovo, Shtip, Vinica, Bogdanci, and Gevgelija, from January to July 2013. The participants were randomly selected on the street, in classrooms, in coffee bars, at their homes, in the business organizations, healthcare institutions, by phone, via the Internet.

### 5.2. Researching subject and statistical analysis

The study included 410 medically educated participants, aged of 18 to 65. The obtained data were statistically and mathematically processed with MS Excel 2010, following statistical and mathematical methods and tests: relative numbers, comparative analysis, proportions, chi-square tests. The data were processed and displayed in tables and graphs.

## 6. Findings

The research interviewed a total of 410 respondents, students of ongoing education or graduated medical education, regardless of their employment state (employed / unemployed). Of the total number respondents, according to the age, the most common age group, was 18 to 20, with 203 respondents (49.5%), followed by the age group of 21 to 30 with 81 (19.8%). In both groups, the majority of the respondents were students. Next was the group aged 41 to 50 with 47 respondents (11.5%), etc.



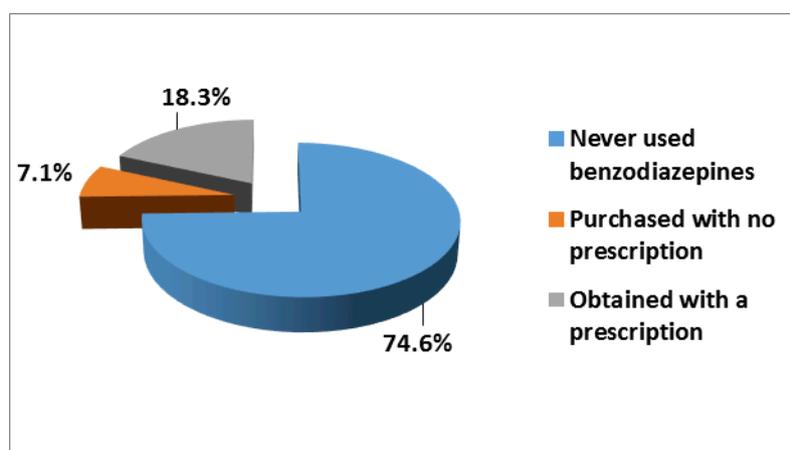
**Figure 01.** Structure of respondents according to gender and the use of benzodiazepines

Of the total number of 410 respondents (Figure 01.), users of benzodiazepines were 104 (25.4%), while 306 (74.6%) were nonusers. Of the total number of 104 users of benzodiazepines, according to the gender, there were 28.1% male users and 71.9% female users. The statistical analysis of the data confirmed that  $X^2=15.324$ ,  $p>0.05$ , led to the conclusion that there were no statistical association, between the gender and the number of (medically/health educated) respondents - users of benzodiazepines.

**Table 01.** Relations of the most common reasons / indications for using benzodiazepines, the number of respondents-users respectively the reason and the number of nonusers

Reason/Indication for using benzodiazepines	Number of users for the	
	listed reason	%
Anxiety	14	3,5
Panic attack (stress)	27	6,6
Insomnia	25	6,1
Convulsions (seizures) or seizures	1	0,2
Pain	8	1,9
Skeletal muscle spasms	3	0,7
Alcohol withdrawal	0	0,0
No particular reason	5	1,2
Various family and/or environmental problems	21	5,2
Never used benzodiazepines	306	74,6
<b>Total:</b>	<b>410</b>	<b>100,0</b>

The research results (Table 01.) showed that most common reasons for the use of benzodiazepine stated by the respondents were: stress - 27 (6.6%) and insomnia - 25 (6.1%), then various family and/or environmental problems - 21 (5.2%), etc. Related to these data and considering the total number of respondents (104) i.e. users of benzodiazepines, the percentage respectively shifts toward higher values as follows: stress (26.0%), insomnia (24%), anxiety (3.5%), etc.



**Figure 02.** Distribution of respondents according to responses of the way of obtaining benzodiazepines

The results of this study (figure 02.) confirmed that the percentage of respondents who got benzodiazepines with a prescription is higher, 75 (18.3%), than those without a prescription, 29 (7.1%).

However, in relation to these data considering to the respondents - users of benzodiazepines it is noticeable that 27.9% (approximately 1/3) of respondents obtained medicines without a prescription (by displaying an identification card of any medical or health association). The largest percentage of respondents believed that benzodiazepines were easily accessible in pharmacies without prescription, 131 (31.9%), but a number of 169 respondents, (41.2%) did not know whether it was possible to obtain benzodiazepine in the pharmacies only at the request of the patient and without prescription from a doctor.

The results of the data analysis of the respondents, attitude regarding the issue use of benzodiazepines during pregnancy and lactation showed that all men (100%) did not answer that question, but all women, 28 (100.0%) think, they could be used without any consequences during pregnancy and breastfeeding. Considering the result of  $X^2 = 12.181$ , ( $p < 0.05$ ), it is deducible that there was a statistical association or connection in terms of the gender of the medically educated individuals and their attitudes related to the question: "May the benzodiazepines be used during pregnancy and breastfeeding"?

**Table 02.** Structure of respondents regarding the use of benzodiazepines and driving / operating motor vehicle/ machine

Answers:	Respondents	
	Number	%
Yes	19	4,7
No	85	20,7
Nonuser of benzodiazepines	306	74,6
<b>Total</b>	<b>410</b>	<b>100,0</b>

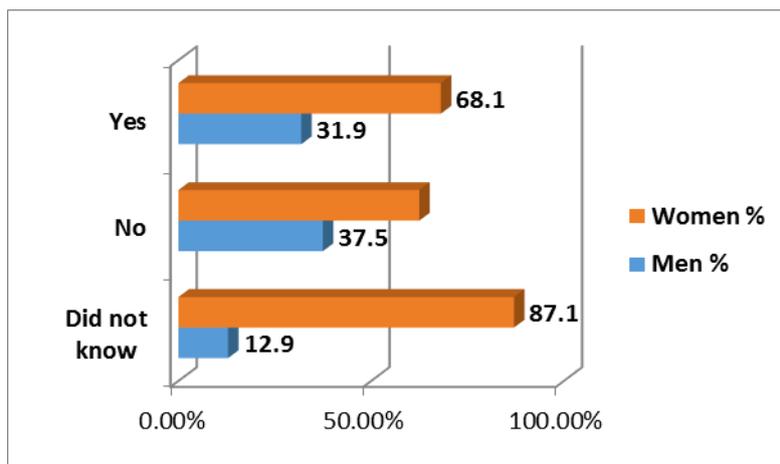
Regarding the total number of respondents (table 02.), the number of benzodiazepine users 19 (4,7%) considering that benzodiazepine consumption was without any consequences on motor vehicle operating, was not great.

**Table 03.** Determination of the statistical significance among gender and attitude for the consumption of benzodiazepines during driving

Attitude for the of the benzodiazepines' use during driving, by gender (cross-data)	fi	fo	(fi-fo)*(fi-fo) / fo
Men (allowed)	80	70,7907	1,1980
Female (allowed)	173	182,2092	0,4654
Men (not allowed)	0	3,3576	3,3576
Female (not allowed)	12	8,6423	1,3044
Men (do not know)	35	40,8515	0,8381
Female (do not know)	111	105,1484	0,3256
<b>Chi-square test:</b>			<b><math>X^2 = 7,4894</math></b>

fi-examined frequency; fo-expected frequency;  $X^2$  - chi-square test;

To the question (table 03.): "Is there any hazard to the concentration and reflexes on using benzodiazepines while driving"? 285 i.e. the biggest percentage (69.5%) answered affirmatively. However, 114 (27.8%) did not know whether there was such a danger. The calculated result of the chi-square test was:  $X^2=7.4894$ ,  $p<0.05$ , and led to the conclusion that there was a statistical association or linkage between the gender and the attitudes related to the previous question.



**Figure 03.** Distribution of responses by gender about the participants' view of whether benzodiazepines can cause psychic and physical dependence

The majority of the respondents (figure 03.), 301 considered that benzodiazepines could cause psychic and physical dependence. Such an attitude was more prevalent among women, 205 (68.1%). About 1/3 of the men, 96 (31.9%) had the same attitude. This question was negatively answered by 24 respondents (62.5% of women and 37.5% of men), who considered that benzodiazepines did not cause psychic and physical dependence. Even bigger was the number of the respondents (85), and mostly women, 74 (87.1%) unknowing whether benzodiazepines caused any dependency.

**Table 04.** Determination of statistical significance among the gender and attitude of respondents whether benzodiazepines may cause psychological and physical dependence

The attitude of the respondents whether benzodiazepines may cause psychic and physical dependence, by gender (cross-data)	fi	Fo	(fi-fo)*(fi-fo)/fo
Men (yes)	96	84,781	1,4846
Women (yes)	207	218,219	0,5767
Men (no)	0	4,197	4,197
Women (yes)	15	10,803	1,6305
Men (do not know)	19	26,022	1,8948
Female (do not know)	74	66,978	0,7361
<b>Chi-square test :</b>		<b>X<sup>2</sup> = 10,5200</b>	
<b>fi- examined frequency; fo-expected frequency; X<sup>2</sup> - chi-square test;</b>			

Since the results of statistical analysis were:  $X^2=10.5200$ ,  $p<0.05$  (table 04.), it was conclusive that there was a statistical association or linkage between the gender of the medically educated individuals and their attitudes related to the question: "Do you think that benzodiazepines can cause psychological and physical dependence"?

To the question of whether they are consuming alcohol during benzodiazepine therapy, the highest percentage answered negatively 123 (30.0%). Only 1 person answered that they were consuming alcohol in the same time during benzodiazepines' therapy (0.9%), while only 3 (2.9%) respondents reported consuming alcohol for reinforcement of the action of the benzodiazepines' therapy.

Of the total number of 104 respondents on the benzodiazepine therapy, 46 (44.2%) discontinued therapy abruptly and only 6 persons (13.0%) reported, that they felt symptoms similar to those characteristic for withdrawal crisis. Certain number of respondents, 16 (15.4%), without physician's consultation / recommendation, had by themselves increased the daily dose of benzodiazepines. Of those who abused benzodiazepines only 4 (3.8%) turned for medical help. A smaller part of the medical / health educated persons, 67 (16.3%) were completely informed of the effects of the benzodiazepines. A large percentage of them, 354 (86.3%), still needed wider public information for the benzodiazepines use and abuse.

**Table 05.** Statistical significance among the gender and attitudes of respondents about certain questions in the questionnaire (cross-data)

<b>Statistical significance (cross-data)</b>	<b>N</b>	<b>df</b>	<b>X<sup>2</sup></b>	<b>p-value</b>
Attitudes related to gender, to the question: "May benzodiazepines be used during pregnancy and breastfeeding?"	<b>104</b>	<b>103</b>	<b>X<sup>2</sup> = 12.181</b>	<b>&lt;0.05</b>
Attitude for the use of benzodiazepines during driving, by gender	<b>104</b>	<b>103</b>	<b>X<sup>2</sup> = 7,4894</b>	<b>&lt;0.05</b>
Among the gender and attitude of respondents, on whether benzodiazepines may cause psychic and physical dependence	<b>104</b>	<b>103</b>	<b>X<sup>2</sup>=10.5200</b>	<b>&lt;0.05</b>

**n-number of respondents; df -degree of freedom; X<sup>2</sup> - chi-square test; p-value**

There is a statistical significance( $p < 0.05$ ), (table 05.), as cross-level data between sex and certain questions in the questionnaire: whether benzodiazepines may be used during pregnancy and breastfeeding, used during driving, whether they can cause psychological and physical dependence.

## 7. Conclusion

According to age, of the total number of 410 respondents, most represented were the age groups of 18 to 20 (49.5%), mostly comprising students aimed to assess whether students, during their medical/health education acquire the most important information about the consequences of use of benzodiazepines and to determine whether health professionals, who have completed medical degree and had some working experience consult with the psychiatrics prior the use of benzodiazepine drug or use them by their own opinion. The determination was in sense of their choice and without prior consultation. In their study, the authors (Spanemberg et al., 2011) aimed to compare the results of use and prescribing of psychotropic medicines emphasizing benzodiazepines. This was done within two groups of patients (one composed of elderly patients and the other composed of young patients), who turned for help in the Emergency Centre of a university hospital for psychiatric consultations. They come to conclusion that there is high prevalence of use of benzodiazepines within elderly patients in the psychiatric emergency services.

In our study, 25.4% were using benzodiazepines. In a private college in England (Sweeney, 2010, p. 2), a hundred students at the age of 18 to 22 were surveyed with the purpose to estimate the use of drugs – stimulants. Here, high rates of usage (56%) of the surveyed students were noticed during their stay in the college. Compared to gender, the percentage ratio between men and women, was 28.1% to

71.9%, which led to a conclusion that both genders believed in the effectiveness of benzodiazepines in a need to relieve stress and insomnia, as the most common reasons presented by the respondents. Another study in the Republic of Macedonia (Mirchevska et al., 2014), confirmed that non-medical persons use benzodiazepines in a higher percentage (81.53%) than the medical. According to the gender of the respondents - users, women use more (58.16%) than men.

The most common reasons for use of benzodiazepines in the Republic of Macedonia are stress (26.0%), insomnia (24.0%) and the presence of various problems in the family and surrounding. These are also the most common causes in other communities outside the Republic of Macedonia, according to many studies. Within the group of non-medical persons (Mirchevska et al., 2014), the most common reason for the use of benzodiazepines is insomnia (18.3%), followed by stress (14.16%), etc. Similar results were obtained also in other studies (Macan et al., 2000; Kapczinski et al., 2001). A previous study conducted on the territory of the Republic of Macedonia concluded that 10.1% of the respondents - pupils used illicit substance at least once in a lifetime, while approximately 6% of pupils had used tranquillizers (anti-anxiety drugs) once or twice (Mugosa, Djuriscic, & Golubovic, 2008).

All medically educated respondents, were most often procuring their benzodiazepines with a prescription (18.3%), which is a positive indicator. However, the percentage of respondents - users of benzodiazepines who bought benzodiazepines without prescription (by displaying an identification card of any medical or health association) were 27.9%. In the study conducted in the private college in England (Sweeney, 2010, p.2), the authors concluded that even though students considered these drugs harmless, from ethical aspect they are physically harmful for those using them without prescription. The completion of this study was followed by positive statutory regulations prohibiting the procurement of these (and many other groups of) drugs without a prescription and introducing strict inspection of their dispensing in the pharmacies by the Ministry of Health. These amendments contributed for overcoming the irregularities in the use of benzodiazepines.

It was evident that both genders, did not have enough information on the harmful effects of the use of benzodiazepines during pregnancy and breastfeeding. In other previous research, data analysis of non-medical persons, for the use of benzodiazepines during pregnancy and breastfeeding, showed that 79.10% were not informed about that (Mirchevska et al., 2014). The use and the effects of benzodiazepines during pregnancy and lactation have also been investigated by other authors (Bergman et al., 1992).

What is favourable in this research is that despite the abrupt discontinuation of use of benzodiazepines to (44.2%) respondents, a lower percentage (13.0%) felt some symptoms similar to those characteristic for withdrawal crisis. Other studies have confirmed similar state (Olfson & Pincus, 1994). To the question of "whether there is danger in the concentration and reflexes when using benzodiazepines while driving", 1/3 (27.8%) did not know whether there was such a danger. Respondents who took benzodiazepine (104) and were driving a motor vehicle - 19 (18.3%) did not have any disturbance in the driving process. A previous study confirmed that a large percentage (57.3%) of non-medical persons, regarding the use of benzodiazepines and driving motor vehicle and / or machine operating, considered no impact on the concentration and reflexes of the operator (Mirchevska et al., 2014). Yet, another prior study indicated, that there was no clear evidence linking the use of benzodiazepines and severity of any damage during driving. Clearly, there is insufficient public

awareness on the issue. Considering everything so far presented, it is necessary to do more research to clarify these issues (Smink et al., 2010).

To the question of whether benzodiazepines were able to cause psychical and physical dependence, a higher percentage of women (68.1%) answered affirmatively, about 1/3 (31.9%) of men had the same attitude, while 20.7% of the respondents (women in higher proportion) did not know. The conclusion that there was statistically significant association between gender and attitudes related to this issue was confirmed by the calculated  $\chi^2$  – test ( $p < 0.05$ ). Those respondents who responded by "no" and "do not know" were not sufficiently informed whether benzodiazepines may cause any dependency. In an earlier research, non-medical persons at higher percentage (78.18%) responded that benzodiazepines might cause dependence (Mirchevska et al., 2014). Similar results were also obtained by other authors in other studies (Longo & Johnson, 2000; Longo, et al., 2000; Uzun, et al., 2010).

It is worrying, that 15.4% of the respondents without consulting a physician, increased their daily benzodiazepine dose, and 44.2% abruptly discontinued their benzodiazepine therapy. Consequently, a small percentage of respondents (3.8%) usually only once (5.8%), turned for medical help. The authors Bursztajn & Brodsky (1997) analyse, that the ethical and legal dilemmas which derive as problems from the clinical practice should be solved, especially if it is about estimating and treating various vulnerable groups. Taking into consideration, that many alcohol and drug addicts abuse benzodiazepines, it is necessary to conduct a psychiatric examination, screening of presence of substances, as well as observance of the bio-psycho-social signs, to discover possible abuse. The author of a study: "Analyses the use and abuse of substances which cause addiction" (Williams, 2007), concluded that this problem, can be one of the most difficult ethical problems to solve within the student population. Furthermore, he considers that, there is not a definite direction which indicates the best advice to the students, when it comes to drugs, narcotics or alcohol.

This research confirmed that medically educated persons in high percentage (25.4%) use benzodiazepines, and despite their medical/health education there is a need of wider public information of the benzodiazepines use and abuse. This attitude refers more to the student population studying at the medical educational institutions and needs broader information on certain issues, which are part of the questionnaire, particularly of the harmful effects of the use of benzodiazepines during pregnancy and breastfeeding, during driving and machine operating, in concomitant alcohol consumption, etc. In our society women use benzodiazepines 2.5 times more than men, and if we analyze the reasons, why these drugs are commonly used it can be concluded that this situation arises from the fact that women are too much burdened since they are employed, but also with plenty of obligations related to the family. It is positive, that today the sale of benzodiazepines is controlled by the state and their abuse is less likely. Considering that data analysis, showed that the awareness of participants on the effects of the use or abuse of benzodiazepines is in a lower percentage, especially among the student population, there is a necessity of greater inclusion of ethical educational content from this area into study programs, and wider campaign by making the promotional health educational materials for pregnant women, drivers, adolescents and the general population, in order to improve the health condition within the population.

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